REMARKS

Claims 1-2, 12, 23, 26, 38, and 47-56 are pending. Claims 3-11, 13-22, 24-25, 27-37, and 39-46 are canceled. Claims 47-56 are newly added.

1. Claims 1, 2, 12, 23 and 38 were rejected under 35 U.S.C. 102(b) as being anticipated by Ruys (Article entitled "Silicon-doped Hydroxyapatite"). Applicants respectfully traverse this rejection.

Present claim 1 is directed to a bioactive artificial sintered composition for supporting bone cell activity. The composition consists essentially of a stabilized tricalcium phosphate and hydroxyapatite in a ratio of at least 50:50 tricalcium phosphate: hydroxyapatite. The stabilized tricalcium phosphate is stabilized with a stabilizing entity selected from the group consisting of silicon entities, aluminum entities, barium entities, titanium entities, germanium entities, chromium entities, vanadium entities, niobium entities, boron entities, and mixtures thereof. The composition is bioactive to support osteoblastic bone growth and to support extracellular resorption of the composition by osteoclasts.

The PTO asserts that the material of Ruys is the same as that claimed and would inherently have the properties and *in vivo* response as claimed. Further, the PTO asserts that Applicants have provided no evidence that would suggest that their composition is any different from that disclosed by Ruys and thus, the PTO maintains its inherency assertions. As reported in the accompanying Declaration by Dr. Timothy J. N. Smith, Applicants have attempted to faithfully perform the experiments outlined in Ruys, but have been unable to reproduce the results reported by Ruys. In particular, Ruys is silent regarding the parameters and methods used for particularly important processing steps and Applicants have been unable to ascertain, through several months of experimentation, which parameters and methods would lead to the results reported by Ruys. Thus, the Ruys reference is incomplete and non-enabling and this rejection over Ruys should be withdrawn on this basis alone. Please see the Rule 132 Declaration by Dr. Timothy J. N. Smith, filed herewith, for additional details.

In any event, turning to the reference, Ruys presented work to determine the feasibility of chemically doping hydroxyapatite with silicon. At all silicon levels hydroxyapatite (HAp)

formed and, at high silicon levels, α-tricalcium phosphate (α-TCP) and Si-P-O glass formed. (Ruys Abstract). In particular, "both α- and β-TCP were formed, although β-TCP was favoured at low silicon levels and α-TCP was favoured at high silicon levels. Further, at higher silicon concentrations, a broad X-ray diffraction peak with a *d* spacing of 0.16-0.26 nm formed. Since both silicon and phosphorous are oxide glass formers, this peak is likely to result from the presence of a Si-P-O glass. For progressively higher silicon levels, the glass became the dominant phase. At very high dopant levels, approximate area ratios of the main diffraction peaks of HAp and TCP suggested that the TCP content was slightly greater than the HAp content." (Ruys, page 77, paragraph 3). As such, Ruys discloses that at high silicon levels the TCP content was slightly greater than hydroxyapatite content, but the Si-P-O glass phase was the dominant phase.

High levels of Si-P-O glass and in particular, high levels of silicon outside of the crystal matrix of the calcium phosphate species limits the activity of osteoclasts and osteoblasts. As described in the accompanying Declaration, high levels of silicon produce a material that limits initial cell attachment to the surface. Thus, the composition disclosed by Ruys does not necessarily and thus, does not inherently have the same *in vivo* response as the claimed materials. In particular, the Ruys material does not *consist essentially of* a composition that has a high content of TCP and is bioactive, since high TCP content materials of Ruys contain notable Si-P-O glass, significantly compromising the bioactivity of the material in terms of osteoblast and osteoclast activity. In this regard, Applicants have found that external Si-containing phases, such as Si-P-O glass, in amounts greater than 20 wt% compromise bioactivity as claimed, that is, "to support osteoblastic bone growth and to support extracellular resorption of said composition by osteoclasts."

In contrast, Applicants have discovered a method for producing bone replacement compositions predominantly formed of stabilized calcium phosphate phases without the formation of a significant amount of silicon compounds outside of the calcium phosphate matrices. As noted in the Declaration, the method is significantly different from the method disclosed in Ruys, and the material produced by such a method is different from the material of Ruys. In particular, the compositions produced by the methods discovered by Applicants are predominantly calcium phosphate compositions and have less than 5 wt% of phases including

silicon compounds other than silicon stabilized calcium phosphate compositions, such as less than about 3 wt% silicon compound phases. As further explained in the accompanying Declaration, the absence of a significant amount of silicon compositions other than the silicon stabilized calcium phosphate compounds in the presence of stabilized α-tricalcium phosphate permits bioactivity and, in particular, permits balanced osteoblast and osteoclast activity as claimed.

New claim 50 recites a bone replacement composition comprising tricalcium phosphate and hydroxyapatite in a ratio of at least 666:333 tricalcium phosphate to hydroxyapatite. Ruys is clearly limited to, at best, TCP content "slightly greater" than the HAp content. A ratio of 666:333 is clearly greater than any ratio fairly derived from the teachings of Ruys.

In summary, the Ruys reference is non-enabling. Further, by its own disclosure, the Ruys reference fails to even remotely suggest a bioactive composition having at least 50:50 tricalcium phosphate to hydroxyapatite. In fact, Ruy teaches the opposite, disclosing that, in compositions in which the amount of tricalcium phosphate is slightly greater than the amount of hydroxyapatite, the Si-P-O glassy phase is dominant and thus, significantly greater than 20 wt% of the composition (See Declaration) and outside the scope of the claimed invention (claim 1). Further, Ruys fails to teach a composition comprising stabilized tricalcium phosphate and hydroxyapatite in a ratio of at least 666:333 tricalcium phosphate to hydroxyapatite (claim 50), let alone a composition with the ratio of at least 666:333 and with insolubility in physiological fluids of pH of 6.4 to 7.3 (claim 55).

For at least the foregoing reasons, claims 1-2, 12, 23, 38, and 47-56 are not anticipated by Ruys. As such, Applicants respectfully request reconsideration and withdrawal of the 35 U.S.C. 102(b) rejection of claims 1-2, 12, 23, and 38.

2. Claim 26 was rejected under 35 U.S.C. 103(a) as being unpatentable over Ruys. Applicants respectfully traverse this rejection.

Claim 26 depends from a claim that is allowable in view of Ruys. In addition, Ruys is silent regarding the morphology and dimensions of granules formed from the claimed composition and fails to provide teaching or suggestion that would motivate one of ordinary skill

in the ceramic arts to form granules of the claimed morphology and dimensions.

For at least the foregoing reasons, claim 26 is patentable over Ruys. As such, Applicants respectfully request reconsideration and withdrawal of the 35 U.S.C. 103(a) rejection.

3. Claims 6, 10, 13, 22, 25, 27, 29, 32, 33, 34, 35, and 37 were canceled, rendering the related rejections moot.

4. Applicants note that previous claim 28 has allowable subject matter and appreciate Examiner Prebilic's statements acknowledging the allowability of the subject matter of claim 28. Applicants have moved the allowable subject matter to claim 56.

5. Claims 47-56 are newly added and include subject matter further patentable over the cited references. In particular, claim 50 is directed to a bone replacement composition comprising stabilized tricalcium phosphate and hydroxyapatite in a ratio of at least 666:333 tricalcium phosphate to hydroxyapatite. The stabilized tricalcium phosphate is stabilized with a stabilizing entity selected from the group consisting of silicon entities, aluminum entities, barium entities, titanium entities, germanium entities, chromium entities, vanadium entities, niobium entities, boron entities, and mixtures thereof.

While Ruys discloses that, at very high dopant levels, approximate area ratios of the main diffraction peaks of hydroxyapatite and TCP suggest that the TCP content was slightly greater than the hydroxyapatite content, Ruys fails to teach or disclose a ratio of at least 666:333 tricalcium phosphate to hydroxyapatite. As such, claims 50-56 are patentable in view of the cited references. In addition, claims 47-49 include subject matter that is patentable in addition to the patentable subject matter of the claims from which they depend.

Applicant(s) respectfully submit that the present application is now in condition for allowance. Accordingly, the Examiner is requested to issue a Notice of Allowance for all pending claims.

Should the Examiner deem that any further action by the Applicants would be desirable for placing this application in even better condition for issue, the Examiner is requested to telephone Applicants' undersigned representative at the number listed below.

The Commissioner is hereby authorized to charge any fees which may be required, or credit any overpayment, to Deposit Account Number 50-3797.

Respectfully submitted,

11.2.07
Date

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